NIDCD National Institute on Deafness and Other Communication Disorders

# 2012-2016 Strategic Plan

HEARING AND BALANCE | TASTE AND SMELL | VOICE, SPEECH, AND LANGUAGE

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# Welcome from the Director

The National Institute on Deafness and Other Communication Disorders (NIDCD) is pleased to share our new five-year Strategic Plan for 2012-2016. The Plan is designed to help the NIDCD prioritize its research funding by identifying areas of outstanding promise, as well as identifying knowledge gaps. By funding research in these areas, NIDCD aims to improve the quality of life for people with communication disorders.

Looking forward, the NIDCD anticipates unprecedented scientific opportunities. We are already using recent advances in science and technology to discover how changes to the molecular, cellular, and systemic pathways can cause communication disorders. The NIDCD hopes to build on these advances by supporting research that will lead to better ways to identify those who are at risk for developing certain communication disorders, with a goal of preventing a disorder from occurring or at least lessening its effects. The NIDCD also continues to support research to develop better treatments for people with communication disorders.

These unprecedented research opportunities are coupled with the challenge of using our best scientific judgment to make difficult choices about which areas of research to pursue. The priority areas in this Strategic Plan have been identified through discussions among outside experts in each of the Institute's mission areas, along with input from NIDCD staff members, the National Deafness and Other Communication Disorders (NDCD) Advisory Council, representatives of the research and advocacy communities, and members of the public.

We thank you for your interest in the NIDCD's scientific research. For more information, please visit the NIDCD website at http://www.nidcd.nih.gov.

Sincerely,

James F. Battey, Jr., M.D., Ph.D.

Director
National Institute on Deafness and Other Communication Disorders

## SCIENCE CAPSULE
## Cochlear Implants

The development of the multi-channel cochlear implant has made it possible to restore the perception of sound to people who are profoundly deaf or severely hard of hearing (HoH). In contrast to hearing aids, which amplify sound, cochlear implants directly stimulate the auditory nerve.

Over the past two decades, NIDCD-supported research led to major advances in multi-electrode signal processing, as well as in understanding the benefits of early implantation in children and the possible benefits of implantation in both ears. Because of this research, we now know that children with hearing loss who receive a cochlear implant within the first two years of life will typically experience a smaller gap in language skills and will be more likely to succeed in mainstream classrooms.

According to the U.S. Food and Drug Administration (FDA), in December 2010, approximately 219,000 people worldwide have received cochlear implants, including approximately 42,600 adults and 28,400 children in the United States. Roughly 40 percent of children who are born profoundly deaf now receive a cochlear implant, which is a 25 percent increase from five years ago. The rise in cochlear implant use among eligible people between 2000 and 2010 exceeded the target set in the U.S. Department of Health and Human Services' (HHS) Healthy People 2010 (a set of science-based 10-year national health objectives), and a new target is being developed for Healthy People 2020.

NIDCD-supported scientists continue to improve cochlear implant technology through the development of noise-reduction signal processing and innovative electrode designs. For example, insertion of traditional cochlear implant electrodes can damage hair cells throughout the cochlea, so researchers are investigating methods to preserve residual hearing in eligible individuals by implanting a shorter electrode array. In addition, animal studies are underway to assess the risks and benefits of a new electrode design that is positioned inside the auditory nerve, with the hope this will provide an improved sense of hearing in crowds and other social situations in which more than one person is speaking. NIDCD researchers continue studies with children who received cochlear implants at a young age to determine what factors contribute to successful language learning and subsequent academic performance. Continued research to assess how current users benefit from a cochlear implant in one ear, along with a cochlear implant or a hearing aid in the other ear, will help inform the design of the next generation of implants.

# Introduction

## NIDCD OVERVIEW

Approximately one in six Americans will experience a communication disorder in his or her lifetime. Communication disorders make the basic components of communication (sensing, interpreting, and responding to people and things in our environment) challenging. In addition, communication disorders not only compromise physical health, but also affect the emotional, social, recreational, educational, and vocational aspects of life. The effects often ripple outward to affect families and social networks, including those at work and school. The total economic impact of these disorders in regards to quality of life and unfulfilled potential is substantial. Furthermore, the prevalence of communication disorders is expected to increase as the population ages, and as survival rates improve for medically fragile infants and people affected by traumatic injuries and diseases.

In October 1988, Congress established the National Institute on Deafness and Other Communication Disorders (NIDCD) (http://www.nidcd.nih.gov) as one of the institutes that compose the National Institutes of Health (NIH) (http://www.nih.gov), part of the U.S. Department of Health and Human Services (http://www.hhs.gov). NIH is the federal government's focal point for the support of biomedical research and is among the leading biomedical research funding institutions in the world. NIH's mission is to seek fundamental knowledge about the nature and behavior of living systems and to apply that knowledge to enhance health, lengthen life, and reduce the burdens of illness and disability. NIDCD's focus within this broad mission is to bring national attention to the disorders and dysfunctions of human communication and to contribute to advances in biomedical and behavioral research that will improve the lives of the millions of people with a communication disorder.

The NIDCD mission is to conduct and support biomedical research, behavioral research, and research training in the normal and disordered processes of hearing, balance, taste, smell, voice, speech, and language. The Institute conducts and supports research and research training related to disease prevention and health promotion; addresses special biomedical and behavioral problems associated with people who have communication impairments or disorders; supports research evaluating approaches to the identification and treatment of communication disorders and patient outcomes; and supports efforts to create devices that substitute for lost and impaired sensory and communication function. To accomplish these goals, the NIDCD manages a broad portfolio of both basic and clinical research. The portfolio is organized into three program areas: hearing and balance; taste and smell; and voice, speech, and language. The three program areas seek to answer fundamental scientific questions about normal function and disorders and to identify patient-oriented scientific discoveries for preventing, screening, diagnosing, and treating disorders of human communication. (Please see *Appendix A* for more information on the NIDCD's funding history.)

The NIDCD accomplishes its research mission through three divisions: the Division of Intramural Research (DIR), the Division of Scientific Programs (DSP), and the Division of Extramural Activities (DEA). The DIR (http://www.nidcd.nih.gov/research) conducts research and related support activities in laboratories and clinics housed at the NIH. The DSP and DEA manage complementary aspects of the NIDCD's Extramural Research Program (http://www.nidcd.nih.gov/funding), a program of research grants, career development awards, individual and institutional research training awards, center grants, and contracts to public and private research institutions and organizations throughout the United States and abroad. As a whole, the Institute supported approximately 1,200 research projects in Fiscal Year (FY) 2011. Through research and education, the NIDCD strives to reduce both the direct and indirect economic burden of communication disorders on individuals, families, and society, thereby improving the quality of life for people living with a communication disorder.

## HEALTH DISPARITIES RESEARCH AT NIDCD

Human communication disorders cross all social and ethnic groups. The NIDCD conducts research to understand the basis of health disparities within its mission areas by determining how communication disorders may contribute to, or be worsened by, differences in health among populations. NIDCD also recognizes minorities and individuals with communication disorders are underrepresented in NIDCD-sponsored research and research training activities and is working to increase participation of individuals and groups from diverse backgrounds. Participation of minority or underserved populations in NIDCD-sponsored research advances the NIDCD mission and ensures that everyone benefits from human communication research. For further details on the NIDCD's efforts in health disparities research, please see the FY 2009-2013 Strategic Plan on Reducing Health Disparities (http://www.nidcd.nih.gov/about/plans/strategic/pages/health_disp.aspx).

## RESEARCH TRAINING AND CAREER DEVELOPMENT AT NIDCD

The number of Americans with communication disorders is expected to increase as the nation's older population increases and as survival rates improve for a wide range of medical conditions associated with communication disorders. In response, the NIDCD has placed an emphasis on research training and career development opportunities to ensure a productive, creative, and innovative cadre of qualified scientists. The NIDCD is continuously adapting its research training and career development efforts to encourage new investigators and build shared research resources. As in health disparities research, the NIDCD recognizes the underrepresentation of various minority and specific populations, such as individuals who are deaf or hard of hearing (HoH), in its research training activities and works diligently to increase participation of individuals from these groups in its training activities to further its research mission, and ensure that all populations are served by human communication research. (More information on training and career development programs is available on the NIDCD website, including support for new investigators in the "NIDCD and Your Research Career" brochure at http://www.nidcd.nih.gov/research/pages/your_career.aspx and on the Support for New Investigators page at http://www.nidcd.nih.gov/funding/apply/pages/new_investigators.aspx.)

The field of human communication sciences needs interdisciplinary research teams of clinicians and basic scientists to bridge the gap between research conducted in a laboratory and active patient care. Clinicians need a deeper understanding of the latest research discoveries to bring new treatments into the clinic. Basic researchers need a more thorough understanding of the needs, challenges, and opportunities faced by clinicians. The cross training of these scientists may help spark new ways of thinking about treatment approaches. Interdisciplinary teams (clinician-researcher M.D., Au.D., and Ph.D.) will be able to initiate and support new directions for scientific discovery, execute hypothesis-driven clinical trials, and assess new therapies.

## TRANS-NIH EFFORTS

While the NIDCD focuses its research efforts on programs that support its mission areas, breakthroughs in related fields (such as neuroscience, genetics, and animal models) improve our understanding of communication disorders. In order to support these discoveries, the NIDCD participates in many Trans-NIH initiatives and programs. (Please see *Appendix B* for examples of some of these Trans-NIH activities.)

## NIDCD STRATEGIC PLAN OVERVIEW

The NIDCD Strategic Plan (Plan) is a guide for the Institute (including NIDCD staff and the NDCD Advisory Council) to prioritize research investment. The NIDCD uses the Plan as a tool when nominating investigator-initiated research applications for High Program Priority (HPP) funding, and when developing Funding Opportunity Announcements (FOA). Furthermore, NIDCD staff distribute the Plan to the research community at workshops or research conferences to increase awareness of Institute priorities. Investigators may submit applications for research projects that directly address priorities within the Plan. Finally, the Plan informs the public about the state of the science and advances in diagnosis and treatment of communication disorders, while creating a vision for the future.

The NIDCD must prioritize its research investment in the areas of training, prevention, diagnosis, and treatment to meet public health needs and explore new opportunities presented by recent scientific progress. To develop the 2012-2016 Plan, the NIDCD convened a series of working groups and solicited input from scientific experts, the NDCD Advisory Council, NIDCD staff, and the public. (Please see *Appendix C* for more details on the Plan process.)

# Future Directions in NIDCD Program Areas

In consultation with communication research scientists and the public, the NIDCD has identified four Priority Areas that have the potential to increase our understanding of the normal and disordered processes of hearing, balance, taste, smell, voice, speech, and language and to further our knowledge in human communication sciences. They are:

## PRIORITY AREA 1

**Understanding Normal Function:** Deepen our understanding of the mechanisms underlying normal function of the systems of human communication. By defining what is normal in both animal models and humans, we can better understand mechanisms of disease.

## PRIORITY AREA 2

**Understanding Diseases and Disorders:** Increase our knowledge of the mechanisms of diseases, disorders, and dysfunctions that impair human communication and health. Understanding mechanisms that underlie diseases and disorders is an important step in developing better prevention and treatment strategies.

## PRIORITY AREA 3

**Improving Diagnosis, Treatment, and Prevention:** Develop, test, and improve diagnosis, treatment, and prevention of diseases, disorders, and dysfunctions of human communication and health. Diagnosis considers normal function and provides targets for prevention and treatment. Improvements in prevention and treatment lead to better outcomes with fewer side effects.

## PRIORITY AREA 4

**Improving Outcomes for Human Communication:** Accelerate the translation of research discoveries into practice; increase access to health care; and enhance the delivery, quality, and effectiveness of care to improve personal and public health. Scientifically validated prevention and treatment models will lead to better personal and public health only if they are translated effectively into routine practice.

Although the Priority Areas described in this Plan help the NIDCD identify promising scientific opportunities to advance human communication research over the next five years, the NIDCD will continue to fund as much meritorious research as possible within our program areas of hearing and balance; taste and smell; and voice, speech, and language.

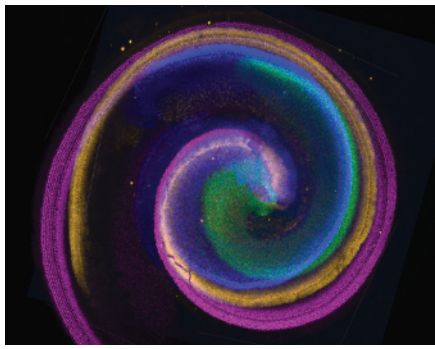
The Plan is not a comprehensive list of all research areas that NIDCD is currently supporting or plans to support in the future. Basic and clinical research being supported by NIDCD will continue to be given high priority. The NIDCD is committed to supporting new, innovative, hypothesis-driven, meritorious research, which can lead to improving the overall health and quality of life for people with communication disorders.

# Hearing and Balance Research

## Why NIDCD Supports Hearing and Balance Research

Hearing and balance disorders decrease quality of life, cross all ethnic and socioeconomic lines, and impose a significant social and economic burden upon individuals, their families, and the communities in which they live. Millions of Americans experience a hearing or balance disorder at some point in their life, especially as young children or older adults. Common examples include otitis media (middle ear infections), noise-induced hearing loss, tinnitus, age-related hearing loss, dizziness, and vertigo. Approximately 36 million American adults report some degree of hearing loss[1] and almost eight million adults report a chronic problem with balance.[2] In addition, two to three out of 1,000 babies born in the United States each year have a detectable hearing loss[3, 4] that can affect their speech, language, social, and cognitive development.

## MOUSE MODELS



Mouse models of hereditary hearing impairment have been and continue to be instrumental in mapping and cloning many of the gene mutations that contribute to deafness. They are also being used to study how gene mutations affect protein function and result in deafness, and to test therapeutic approaches to treat or prevent hearing loss. These models allow researchers to study genetic factors involved in hearing loss and the development and maintenance of the human ear. In addition, mouse models have allowed scientists to directly examine auditory sensory cells and to characterize the inner ear's response to sound. Recent research has identified some of the cellular processes that contribute to hair cell damage and death, allowing future studies that may determine the inner ear's response to mechanical and chemical trauma.

## OTITIS MEDIA

Otitis media (OM), or middle ear infection, is a condition that affects most young children prior to three years of age. Repeated episodes of OM can contribute to hearing loss and a possible delay in language and cognitive skills development. NIDCD research is improving our understanding of susceptibility and pathogenesis of OM. In the future, this research might define immune pathways for effective middle ear protection by vaccines.

## TINNITUS

Tinnitus, or ringing in the ears, is a hearing disorder that affects approximately 25 million Americans, both those with and without hearing loss. Its severity can range from a mild condition, which requires no intervention, to a severe debilitating disease with significant emotional, social, and economic impact. NIDCD research aims to determine the neural basis of tinnitus, and to develop effective interventions for affected people.

## TECHNOLOGY INTERVENTIONS FOR HEARING LOSS

People with mild to moderate hearing loss often benefit from using a hearing aid, and many with severe to profound hearing loss benefit from being fitted with a cochlear implant. Advances in both hearing aid and cochlear implant technology are improving the ability of both types of devices to treat many people with various types of hearing loss. For example, individuals may be fitted with hearing aids or cochlear implants on both ears instead of only one ear to improve sound localization and discrimination. In recent years, some people with residual hearing for low-frequency sounds have received both a cochlear implant, to aid them in hearing higher-frequency sounds, and a hearing aid to allow them to take advantage of their residual low-frequency hearing. In many cases, this strategy results in a significant improvement in hearing performance over the use of only one device.

## BALANCE DISORDERS

The inner ear contains the vestibular system, which helps us maintain our balance and navigate. Vestibular disorders lead to dizziness, vertigo, nausea, migraines, and various forms of postural instability. Dysfunctions of the vestibular system can occur independently or with a hearing loss. NIDCD research is supporting the development of safer, better tolerated, and more effective pharmacological treatments for vertigo. Additional research is attempting to develop vestibular prosthetic devices and minimally invasive surgery techniques to control imbalance and vertigo while preserving hearing and other functions.

## THE HEARING AND BALANCE PROGRAM

The NIDCD Hearing and Balance Program encompasses over half of NIDCD's portfolio. To study normal and disordered functions of the auditory and vestibular systems, the NIDCD employs a wide range of research approaches such as molecular genetics, cellular biology, animal models, biomedical imaging, nanotechnology, psychoacoustics, and structural and functional biology. The NIDCD supports research that will lead to improved treatments for, and prevention of, hearing and balance disorders.

# Recent Advances in Hearing and Balance Research

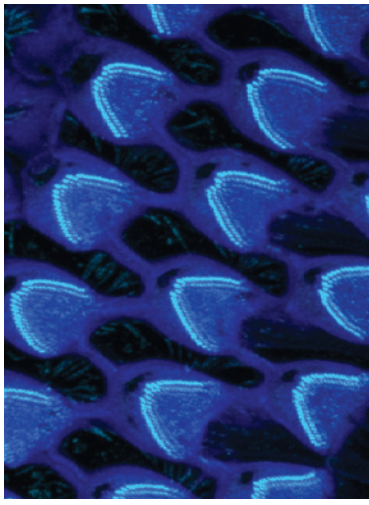
## HAIR CELLS

- Identification of molecular components of tip links,[5] function of TRIOBP,[6] and activity of stereocilin[7] has advanced understanding of hair cell transduction, the pivotal point at which hair cells convert sound vibrations into an electrical signal.

- Recent biophysical characterizations of the molecular motor prestin that drives outer hair cell electromotility, including its interactions with cytoskeleton, anions and membrane constituents,[8-10] have led to a deeper understanding of how this cell provides for mammalian cochlear amplification,[11, 12] the metabolically vulnerable process that boosts our ability to hear so well.

- Researchers have generated hair-like cells from both mouse embryonic stem cells and mouse induced pluripotent stem cells (iPSCs), providing hope that similar hair cell-like cells can be generated from human stem cells.[13]

- Advances in DNA sequencing, genetics, and protein purification have helped identify molecules essential for sound sensation, which may offer the possibility of specific treatments for individual defects.[6, 14-16]



## HEARING LOSS

- Dozens of new gene defects in hereditary hearing loss have been identified in recent years to better predict the course of hearing loss and develop therapeutic interventions.
- New analyses of national epidemiologic data suggest that the prevalence of hearing loss may have stabilized or could even be in decline.[17, 18] Accurate estimates of these trends are critical, given their long-term implications for public health and health care systems.
- Adenoviral vectors have introduced a growth factor, called brain-derived neurotrophic factor (BDNF), within the cochlea of guinea pigs.[19] This approach may improve survival of the auditory nerve in a cochlea without hair cells, or regrow auditory nerve fibers to be stimulated by the electrodes of a cochlear implant.
- A Phase III clinical trial concluded that injecting steroids directly into the middle ear was comparable to oral prednisone in treating sudden sensorineural hearing loss, a key finding for people who cannot take oral steroid therapy because of diabetes, hypertension, or other conditions.[20]

## OTITIS MEDIA

- Research has advanced understanding of the innate immune system, cell signaling, and gene expression patterns in OM.[21]
- Genome sequencing of middle ear pathogens has identified genes important for virulence and disease progression, as well as potential vaccine candidates.[22-25]
- Several new mouse strains with spontaneous chronic OM have been characterized and the individual mutations identified. These models will further our understanding of the genetic, morphological, and functional abnormalities of this disorder in the middle ear and eustachian tube.[26, 27]

## BALANCE DISORDERS

- Increased understanding of comorbid relationships among balance disorders, migraine, and anxiety will lead to better therapies.[28]
- The effectiveness of canal repositioning maneuvers for the treatment of benign paroxysmal positional vertigo (BPPV) has been established, offering clinicians a range of choices in selecting the treatment best suited to a person's needs.[29]
- The development of a vestibular prosthesis from a re-engineered commercial cochlear implant provides a means of stimulating the semicircular canals, which are part of the vestibular system. The prosthesis could act as a treatment for Ménière's disease and other balance disorders.[30]

## HEARING AIDS AND IMPLANTABLE HEARING DEVICES

■ Advances in the digital technology of hearing aids provide noise reduction, directional hearing, and feedback suppression. Binaural hearing aids further improve sound source localization and spatial separation.[31] Combined use of a hearing aid and a cochlear implant (in opposite ears or the same ear) helps communication more than either device alone.[32]

■ Research in pediatric cochlear implants has identified an age range in which the auditory system is most sensitive to electrical stimulation.[33]

■ Infrared cochlear nerve stimulation and intra-nerve electrodes are experimental cochlear implant designs that offer more precise stimulation of specific nerve sites.[34]

■ The auditory brainstem implant (ABI) stimulates the part of the brain that processes sound. It is typically used in cases where the auditory nerve has been surgically removed due to tumor growth, such as in people with neurofibromatosis 2 (NF2). Recently, use of the ABI has been expanded to other adults[35] and children,[36, 37] some of whom approach performance levels similar to cochlear implant users.

■ The use of binaural cochlear implants has improved directionality and performance in noise.[38, 39]

## TINNITUS

■ Abnormal brain activity of auditory and non-auditory areas is involved in the perception of, and negative reaction to, tinnitus. New therapies will use brain stimulation to treat tinnitus.[40, 41]

■ The use of vagus nerve stimulation paired with a variety of tones over an extended period has been effective in the treatment of noise-induced tinnitus in an animal model.[42]

## AUDITORY PROCESSING

■ Advances in brain imaging along with behavioral studies of auditory perception have increased our understanding of real-world auditory processing and of various auditory neuropathies.[43-45]

■ The integration of auditory activity with other sensory systems (balance, movement and body position, vision) and cognitive function (learning, memory, attention) has advanced understanding of normal and abnormal auditory function in the real world.[46]

■ Electophysiologic studies of adults with normal hearing have revealed that stimulus-specific cues in auditory training can be detected physiologically,[47] indicating that future therapy may be successfully tailored to specific individual needs and abilities.

## SCIENCE CAPSULE
## Hearing Aids and Hearing Health Care

NIH- and NIDCD-supported research has driven the development of hearing aids from the first electronic hearing devices invented in the 1950s to the sophisticated digital devices available today. Innovative collaborations between the NIH, the Department of Veterans Affairs (VA), and the National Aeronautics and Space Administration (NASA) have significantly improved hearing aid technology over the past 20 years. In addition to amplifying sound, today's hearing aids are better designed to address the challenges of understanding speech, localizing sound, and hearing in noisy environments.

Despite these advances, NIDCD-supported scientists are continuing to seek ways to improve hearing aid technology, hearing aid fitting strategies, and auditory rehabilitation programs to enrich the communication experience and quality of life for millions of Americans who have hearing loss. NIDCD-supported scientists are developing more effective methods to reduce sound distortion, improve sound localization, and combine hearing aid and cochlear implant technologies. For example, NIDCD-supported research on the tiny fly named *Ormia ochracea* provided a model for the development of a miniature directional microphone for hearing aids to help users focus on a single speaker in a noisy room.

Improving hearing health is an ongoing priority for NIDCD. An estimated 17 percent of all American adults and nearly half of adults ages 75 years and older have some form of hearing loss, yet only about 20 percent of those who could benefit from hearing aids actually use them. For the past two decades, the NIH and the VA have cosponsored biannual national and international meetings to facilitate information sharing among hearing aid technology researchers. In 2009, NIDCD convened a workshop titled "Accessible and Affordable Hearing Health Care for Adults with Mild to Moderate Hearing Loss," that resulted in research recommendations and a series of NIDCD research initiatives to explore new approaches, assessment methods, and small business technologies to improve access to hearing health care for underserved individuals. In addition, increasing the rate of hearing aid usage was a HHS Healthy People 2010 goal and continues as a Healthy People 2020 goal. NIDCD is committed to pursuing research to understand and improve hearing health for all Americans.

# Priority Areas in Hearing and Balance Research

## 1 PRIORITY AREA
### Understanding Normal Function

■ **Development of the Auditory and Vestibular System:** Identify the molecules and genes involved in development of the peripheral and central auditory and vestibular pathways. Understand how auditory neurons recognize and establish tonotopic organization.

■ **Homeostasis and Microenvironment:** Increase understanding of homeostasis in the inner ear (e.g., ionic composition and maintenance, inflammatory response and toxin elimination, blood-labyrinth barrier, microcirculation, hormonal and other control systems) and in the middle ear (e.g., gas exchange, fluid regulation, innate immunity, and gene expression).

■ **Mechanics:** Expand knowledge of mechanics in the cochlea (e.g., interaction of hair cell membranes and sterocilia with supporting structures); in the middle ear (e.g., resolve important issues of middle ear mechanics, including tympanic membrane/ossicular coupling and the role of non-piston-like modes of stapes motion); and in the vestibular system (e.g., cupular and otolithic maintenance of posture and equilibrium).

■ **Sensory Cell Transduction:** Identify the molecular constituents of hair cell transduction: nanomechanical properties, molecular motors in hair cell membranes and stereocilia, ion channels and pumps; and their integration for hair cell tuning and maintenance.

■ **Cochlear Amplification:** Identify molecular determinants responsible for the biophysical traits that influence amplification, including the basis of its fast kinetics; delineate roles of stereociliar vs. somatic mechanisms in mammalian cochlear amplification; determine roles of amplification in low and high frequency regions of the cochlea; refine mathematical models of amplification and outer hair cell function.

■ **Functional Connectivity:** Clarify how afferent and efferent neural circuits process auditory and vestibular peripheral input. Understand how coding schemes influence plasticity and enable attention, cognition, and stress. Incorporate advanced techniques of functional and structural neural imaging and connectivity, ranging from molecular to systems scale.

■ **Perception:**

- Auditory System: Determine how sound detection, discrimination, and recognition interact with learning, memory, and attention as well as with vision, tactile sensation, and balance to better understand auditory perception in real-world listening environments.
- Vestibular System: Determine how vestibular, visual, and proprioceptive (the sensing of motion or position) systems interact to perceive space and motion and to maintain orientation.

## 2 PRIORITY AREA
## Understanding Diseases and Disorders

■ **Epidemiology:** Investigate natural history; genetic and environmental risk factors; racial, ethnic, and gender differences; and practical objective metrics for subpopulations to inform the development of evidence-based treatment strategies. Explore how complex comorbidities create differences in disease phenotypes and treatment outcomes.

■ **Inherited Disorders:** Identify gene mutations responsible for congenital and age-related deficits, understand structural consequences of such mutations, and develop high-throughput platforms for testing individuals. Understand how specific mutations relate to the severity and progression of disease. Investigate protein function to inform better prevention and treatment strategies.

■ **Otitis Media:** Improve understanding of susceptibility and pathogenesis related to genetics, prior upper respiratory infection, eustachian tube dysfunction and reflux, bacterial biofilms, polymicrobial infections, inflammatory dysregulation, and mucosal hyperplasia. Define immune pathways for effective middle ear protection by vaccines. Determine impact of vaccination on disease prevalence and infection by other microbes.

■ **Inflammatory and Autoimmune Responses of the Inner Ear:** Identify and characterize first responders to injury in the inner ear. Determine how molecules and cells cross the blood-labyrinth barriers to initiate immune response and autoimmune disease. Identify genetic and epigenetic risk factors. Investigate innate and cognate immunity in resolution of OM.

■ **Tinnitus:** Develop new animal models to understand the specific neural deficits responsible for tinnitus.

■ **Other Acquired Disorders:** Improve understanding of the pathogenesis of noise-induced, traumatic, idiopathic, ototoxic, neurotoxic, metabolic, and non-hereditary degenerative auditory and vestibular dysfunction. Improve delineation of the multiple processes resulting in presbycusis. Relate molecular, cellular, and structural (e.g., temporal bone research) otopathology to the clinical progress of disease.

■ **Pathways and Damage:** Determine how the peripheral and central auditory and vestibular pathways are reorganized following injury. Define the long-term changes resulting from early sensory loss. Identify molecular, genetic, and anatomical underpinnings of plasticity. Relate functional deficits to specific lesions in the pathways.

■ **Changes in Perception with Disease:**

- Auditory System: Identify sources of variance contributing to large individual differences in response to similar intervention strategies among people with hearing loss. Improve understanding of the time course, sensitive periods, and complications of hearing loss.
- Vestibular System: Understand how disease affects perception of motion and spatial orientation, including connections with limbic and autonomic systems.

## 3 PRIORITY AREA
## Improving Diagnosis, Treatment, and Prevention

■ **Regeneration:** Develop *in vitro* systems to identify genes and factors that promote regeneration of specific cellular phenotypes (e.g., hair cells, supporting cells, spiral ganglion neurons, cells of the stria vascularis); understand factors that regulate hair cell regeneration; and determine which genes and extracellular factors control cell-specific differentiation.

■ **Pharmacotherapeutics:** Develop targeted delivery of viral vectors for gene therapy and site-specific, controlled, sustained molecular therapy for both developing and dysfunctional pathways. Develop therapies to improve neuronal stimulation, resist cell damage, and enhance cell repair.

■ **Tinnitus:** Apply advanced imaging techniques to provide measures of changed neural activity in people with tinnitus. Identify pharmacologic agents to prevent tinnitus resulting from traumatic, ototoxic, degenerative, and other acquired disorders. Identify behavioral, pharmacological, surgical, and device-based treatments for improving tinnitus.

■ **Otitis Media:** Develop polyvalent vaccines for polymicrobial middle ear infection. Develop new drug delivery systems to the middle ear to prevent development of, enhance innate immunity to, and speed recovery from inflammation. Develop therapies to prevent and treat biofilms.

■ **Interventions for Hearing Loss:**

- Examine existing and develop better aural rehabilitation strategies. Investigate how aural rehabilitation strategies are affected by treating comorbid conditions that influence success, such as dementia, diabetes, osteogenesis imperfecta, and stress.
- Traditional (external) Hearing Aids: Improve device performance in background noise and other real-world settings.
- Cochlear Implants: Improve efficacy of bilateral implants, short electrode implants, and hybrid cochlear implant/hearing aids in the same or opposite ear in conjunction with auditory/aural rehabilitation, assistive electronic devices, sign language, in home and educational environments. Improve prediction of outcome and maintenance of outcome over time.
- Other Implants: Improve efficacy of partially and fully implantable middle ear devices, round window transducers, bone-anchored devices, ABI, and other brain implants.

**Interventions for Dizziness and Balance Disorders:**

- Develop safer, better tolerated, and more effective pharmacological treatments for vertigo.
- Develop vestibular prosthetic devices and minimally invasive surgery for better control of imbalance and vertigo while preserving hearing and other functions.
- Develop improved behavioral approaches for the rehabilitation of chronic vestibulopathies.
- Develop improved methods of systematic diagnosis and delineation of subtypes of dizziness/vertigo in order to identify subpopulations that might respond best to targeted therapies.
- Understand post cochlear implantation dizziness and the connection with vestibular migraines.

**Metrics:**

- Hearing Disorders: Develop metrics that better define functional hearing and communication abilities under real-world listening conditions; differentiate clinical subtypes of hearing disorders; identify early pathology in its preclinical stage; provide better measures of performance, communication skills, and disease-specific quality of life instruments for cochlear implant users; and improve assessment of the perception of, and reaction to, tinnitus.
- Balance Disorders: Develop metrics for the perception of equilibrium, dizziness, vertigo, and spatial disorientation with emphasis on relationships among disequilibrium, emotional disabilities, and cognitive disabilities.
- Identify common data elements to improve communication among scientists and clinicians across different specialties.

**Management of Older Adults:** Improve hearing loss management, including screening, treatment, and rehabilitation. Define the underserved population of older adults for hearing health care. Determine if early access to hearing health care changes health outcomes later in life. Develop and evaluate the effectiveness of screening methods. Reduce risk of falls in older adults due to imbalance. Develop assistive balance aids and training programs to augment stability and posture in the elderly.

**Clinical Trials and Other Clinical Research Studies:** Develop and implement infrastructure to identify 1) investigators with expertise in epidemiology, clinical trials, data registry, and other clinical research and 2) academic- and community-based clinical practice settings with geographic, racial, and ethnic diversity in order to facilitate rigorous, cost-effective clinical research and maximize human subjects protections.

**Emerging Technologies (including Bioengineering, Nanotechnology, and Neural Prostheses):** Capitalize on emerging scientific advances and technologies from nanoscience, biomedical engineering, and other areas to improve treatments and develop novel devices that support impaired function.

**Training:** Promote the cross training of basic scientists, clinician scientists, and physician scientists to facilitate the development of interdisciplinary research teams and to stimulate translational research.

## 4 PRIORITY AREA
## Improving Outcomes for Human Communication

■ **Hearing Health Care:** Identify factors that influence a person's motivation and perceived need for hearing health care. Examine the impact of organization, financing, and management of health care services on the delivery, cost, access to, and outcomes of services. Develop innovative delivery systems, including telehealth and the Internet, to increase awareness, access, and affordability. Identify cost-effective approaches for diagnosis and treatment.

■ **Comparative Effectiveness Research and Evidence-Based Medicine:** Through clinical trials and epidemiological comparative effectiveness research, identify best treatments for a given medical condition for a defined set of individuals. Develop and use clinical registries, clinical data networks, and other forms of electronic health data to inform the conscientious, explicit, and judicious use of current best evidence in making decisions about hearing health care options.

■ **Implementation and Dissemination Research:** Investigate effective implementation of "best practices" among health care providers to translate advances into routine community practice. Increase the effective dissemination of health information to the public to promote healthy behaviors.

■ **Community-Based Participation in Research:** Promote community-based research to identify factors that influence outcomes for people with hearing and balance disorders in diverse real-world settings. Engage deaf and HoH individuals in community-based research to aid in developing behavioral interventions to improve their quality of life. Develop methods to address communication disorders in diverse populations, considering variations in care and practice settings.

# Taste and Smell Research

## Why NIDCD Supports Taste and Smell Research

The chemical senses—more commonly known as taste, smell, and chemesthesis (the "feel" of a chemical; chemically provoked irritation)—enable us to use chemical signals to communicate with the environment and each other. For people, memories of taste and smell experiences are vivid and long lasting, and play an important role in our enjoyment of life. The chemical senses accomplish three major purposes:

- Nutrition: Seeking out safe and nourishing food.
- Protection: Helping us to avoid spoiled food and toxic chemicals.
- Communication: Conveying important information to others.

Specialized cells in the human oral cavity can detect at least five basic taste qualities: sweet, sour, bitter, salty, and savory (umami). Taste cells may also respond to components of fat, to calcium, and perhaps to other chemical substances found in foods and beverages. Together with the nose and oral cavity, the tongue also plays a role in chemesthesis, a multimodal chemical sensitivity whose burning sensations signal the presence of chemical irritants such as capsaicin in hot peppers and toxic chemicals in the air.

Olfactory sensory neurons in the nose can detect a wide array of odors and olfaction (smell) plays an important role in the perception of food flavor as well. In 1991, Linda Buck and Richard Axel described a very large family of about 1,000 mouse genes that give rise to an equivalent number of olfactory receptor types.[48] These receptors are located on olfactory sensory neurons that occupy a small area in the upper part of the nasal epithelium. Drs. Buck and Axel received the 2004 Nobel Prize in Physiology or Medicine for this groundbreaking research, which established a foundation for understanding how odorant molecules interact with their odor receptors.

The prevalence of an impaired sense of smell increases with age, and is generally more prevalent in men than in women. From ages 53-59, approximately four percent of women and nine percent of men demonstrated an impaired sense of smell. By ages 70-79, the incidence is nearly 21 percent in women and 41 percent in men, and is even higher in people ages 80-97: approximately 59 percent in women and 70 percent in men.[49]

Evidence of taste and smell disorders in association with other health problems is increasing. People with early stage Alzheimer's disease and idiopathic (not genetic) Parkinson's disease report a reduced sense of smell, as do people with polycystic kidney disease (PKD). In the United States, about 600,000 people have PKD.[50] Scientists have identified a link between gestational diabetes and an altered preference for sweet foods. Based on an international, multicenter study, gestational diabetes may affect as many as 18 percent of pregnancies.[51]

## NUTRITION

The chemical senses are important for regulating food preferences and intake. They evolved to help humans and other animals survive in environments in which required nutrients were scarce and many plants contained poisonous, bitter compounds. Consequently, we seek out sweet, fatty foods and tend to reject the bitterness that characterizes many nutritious vegetables. Although this behavior made sense as humans were evolving, an almost limitless availability of high-calorie foods today can cause the normal function of taste and smell to lead to overconsumption. Over two-thirds of American adults are overweight, and one-third are obese.[52] Individuals who are overweight or obese are at risk of numerous serious conditions, including:

- type 2 diabetes
- coronary heart disease and stroke
- metabolic syndrome
- certain types of cancer
- sleep apnea
- osteoarthritis
- gallbladder disease
- fatty liver disease
- pregnancy complications[53]

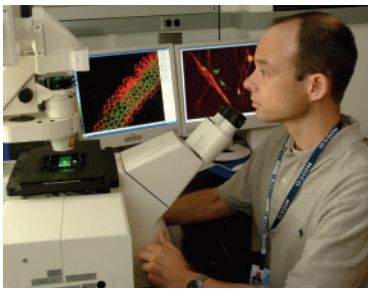
People with smell disorders often have problems appreciating the smell of foods, and claim that food is less enjoyable. They may change their eating habits. Some may eat too little and lose weight, while others may eat too much and gain weight. In either case, there may be a long-term impact on overall health. Loss of the sense of smell may also cause a person to add too much sugar or salt to make food taste better. This can be a problem for people with certain medical conditions such as diabetes or high blood pressure. In severe cases, loss of smell can lead to depression.

Humans seek out their preferred flavors in foods. Flavor involves interactions between the sensors that detect taste, smell, and chemesthesis in our foods and the parts of the brain that interpret, remember, or think about them. Flavor plays an important role in determining whether someone accepts a particular food, and how much of it they choose to eat.[54] Scientists studying the chemical senses are interested in learning more about the molecular and developmental bases for how flavors influence food intake and overall health.

Overconsumption of salt has become an area of particular concern due to the high levels of salt found in the processed foods that comprise the typical modern diet. Historical evidence suggests that human beings have consumed more salt than is physiologically necessary for a long time.[55] Scientists are interested in learning whether there is another undetermined reason for this high salt intake. Too much salt raises blood pressure, and high blood pressure[56] is related to numerous health conditions, including heart disease, kidney failure, and stroke.[56]

Scientists are interested in learning more about how the body detects and responds to salt, fats, and other food characteristics that humans seek out. Data gained from these studies can help us determine new strategies to control overconsumption and improve health without reducing our enjoyment of food. Ongoing research is studying the structure and function of discrete taste, smell, and chemesthetic receptors, as well as their targets within the brain.

## PROTECTION



The chemical senses evolved to help us avoid environmental dangers. Bitter tastes warn of potential toxins. Odors associated with spoiled food, toxic volatiles, and dangerous organisms protect us against ingesting or contacting dangerous substances. Odors can even be used to label certain dangerous substances, such as the addition of smelly sulfur compounds to natural gas, which otherwise has no detectable smell. Chemesthesis primarily serves a defensive function, triggering a coughing or gagging reaction that allows us to avoid chemical irritants that cause tissue damage. Loss of chemesthesis results in the inability to detect toxic chemicals in our environment, possibly leading to increased exposure and greater risk of serious health effects. This loss of detection ability persists in people involved in the early rescue, recovery, demolition, or cleanup efforts after the collapse of the World Trade Center towers.[57] Cancer treatments such as radiation and chemotherapy may also result in taste and smell loss.

## COMMUNICATION

Many animals, including mammals, detect chemical cues (some of which are called pheromones) given off by animals of the same species. These chemicals communicate a variety of messages, including fertility, social rank, health status, and individual identity. Pheromones can also inhibit or induce sexual maturation or mark territory via urination or spraying. Since so many animals use pheromones to communicate information through chemical signals, it seems reasonable to propose that humans do the same. However, the study of chemical communication and pheromones in humans is fraught with controversy. Scientists do not yet agree whether and how humans may use pheromones to communicate. However, other types of odors also affect the way humans interact. For example, people with smell loss may exhibit poor hygiene because they cannot detect their own body odor, thus affecting their normal interactions with others.

## REGENERATION

The cells that detect chemical signals show a remarkable capacity for regeneration. Their locations (in the nose, on the tongue, in the oral cavity) make them susceptible to damage from the environment, so regeneration is required if these cells are to continue to function throughout life. Scientists are interested in learning what enables these tissues to regrow and to re-establish the appropriate connections with the brain. What they learn could be applicable to other human systems and could lead to new treatments for not only taste and smell disorders but also for tissues damaged by stroke or neurodegenerative diseases.

## THE TASTE AND SMELL PROGRAM

The NIDCD Taste and Smell Program supports the study of the chemical senses (taste and smell) to enhance our understanding of how individuals communicate with their environment and how chemosensory disorders can be identified and treated. NIDCD-supported research on molecular and cellular biology, animal models, biophysics, and biochemistry of the olfactory and gustatory systems is paving the way for improved diagnosis, prevention, and treatment of chemosensory disorders.

# Recent Advances in Taste and Smell Research

## TRANSDUCTION MECHANISMS

■ Chemosensory transduction mechanisms—the processes that enable the conversion of detection into an electrical signal—are employed widely throughout the body and are implicated in regulation of digestive[58-61] as well as respiratory functions.[62, 63] New families of chemosensory receptors (TAARs, FPRs) have been discovered that could detect chemical cues used for communication or odors that signal disease.[64, 65]

■ Researchers have discovered diverse receptor cell types and mechanisms in chemosensory transduction in the gustatory (taste) and olfactory systems.[66-69]

## HOW GENES AND ENVIRONMENT AFFECT FOOD PREFERENCE

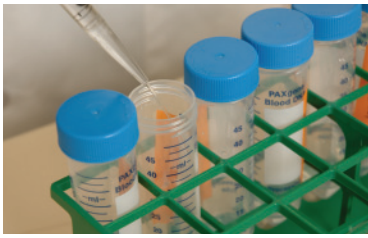
■ Both experience and genetic variation in taste and smell receptor genes affect innate likes and dislikes. Thus, the chemical senses play key roles in the regulation of food intake that underlies major health issues such as obesity and diabetes.[70-73]

■ The discovery that children and adults experience chemical senses differently has broad implications for the role of flavor in diet selection and health across the lifespan as well as for basic research into the organization and maintenance of chemosensory pathways.[72-75]

## CHEMICAL SENSES AND DISEASE

■ Some heritable diseases (e.g., channelopathies[76, 77] and ciliopathies[78]) as well as neurodegenerative diseases (e.g., Alzheimer's disease[79]) have a correlated chemosensory dysfunction that scientists may use to help diagnose diseases or gauge the effectiveness of treatment.

■ Understanding invertebrate chemoreceptor mechanisms and sensitivities has opened avenues for control and prevention of critical insect-borne diseases such as malaria,[80] dengue fever,[81] and encephalitis.[82]



## NEURAL CIRCUITRY

- Researchers better understand the divisions of function in cortical structures that interpret chemical senses information[83] and how these circuits fail in pathology.[79, 84, 85]
- Scientists have gained knowledge of how cortical circuits create and read odor patterns and the basic circuitry and physiology of these circuits.[86-91]
- Artificial neural networks and optical imaging have been used to define and dissect the circuitry and coding in the chemical senses.[92, 93]
- Adult-born neurons can be functionally and synaptically integrated into neural circuits.[94-96]
- Researchers have discovered the circuitry underlying odor-specific behaviors.[97-99]

## SCIENCE CAPSULE
### Olfactory System Detects Bacteria

In addition to detecting smells, our nose conditions the air we breathe: warming, moistening, and cleaning it as it passes specialized sections of nasal lining called respiratory epithelium (RE). The RE also contains solitary chemosensory cells, which detect irritants in the air and send this message to the brain via the trigeminal nerve. One result of trigeminal activation is the ejection of the irritant via a cough or sneeze. NIDCD-supported scientists were surprised, however, to identify chemosensory cells bearing bitter taste receptors (from a group of related genes called T2R) in the RE. This discovery aroused their scientific curiosity—why would cells in the nose need to detect something that *tastes* bitter?

In their attempts to answer this question, the scientists may now have identified a new role for the nose: a first-line defender against disease-causing bacteria. They tested whether the bitter taste-detecting cells responded to special bitter molecules—called quorum sensing molecules—that bacteria use to let each other know when their numbers are high enough to establish a long-term infection. In some cases, the bacteria may form a biofilm, a sturdy bacterial structure that attacks respiratory tissue and is resistant to immune defenses. Using mice, they demonstrated that solitary chemosensory cells in the nose do respond to quorum sensing molecules in concentrations required for forming biofilms, and activate the trigeminal nerve. The trigeminal nerve fiber in the nose then initiates an inflammatory immune response—the blood vessels in the area become leaky to allow white blood cells to attack the bacteria, and the amount of air entering the nose is reduced—to restrict the entry of any new bacteria. In this way, the chemosensory cells in the nose set off the alarm to alert the immune system of a bacterial attack.

The current experiments tested quorum sensing molecules found in mice on mouse T2R-expressing chemosensory cells. The scientists now plan to test whether human T2R-expressing chemosensory cells respond to quorum sensing molecules from bacteria that typically invade the human nose.

# Priority Areas in Taste and Smell Research

In developing research Priority Area goals, the NIDCD took into consideration areas of research that are within the mission of other NIH Institutes, Centers, and Offices (ICO) and are not primarily supported by the NIDCD but that have relevance to the study of chemical senses. In particular:

- **Dietary Intake:** The NIDCD supports basic research on chemosensory factors controlling flavor perception, food selection, and related neural pathways. However, research studies that focus exclusively on the consequences of overconsumption or poor diet, including type 2 diabetes, metabolic disorders, stroke, cancer, cardiovascular disease, hypertension, and obesity, are supported in the mission areas of other NIH ICOs, such as the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), the National Institute of Neurological Disorders and Stroke (NINDS), the National Cancer Institute (NCI), or the National Heart, Lung, and Blood Institute (NHLBI).

- **Infectious Diseases:** The NIDCD supports studies of basic neural mechanisms of insect olfaction, including olfaction of insects that serve as disease vectors for encephalitis, dengue fever, and malaria. However, the funding of studies focusing exclusively on the infectious nature of these diseases falls within the mission of the National Institute of Allergy and Infectious Diseases (NIAID).

## 1 PRIORITY AREA
## Understanding Normal Function

■ **Fundamental Biology of Chemosensory Function:** Continue to develop and apply new tools and approaches to delineate the organization of molecules, cells, and neural circuits underlying the function of the gustatory and olfactory systems.

■ **Peripheral and Central Bases of Flavor:** Understand the complex interactions between peripheral and central aspects of flavor perception, including retronasal or orthonasal olfaction, oral chemesthesis (chemical irritation), taste, oral somesthesis (temperature, texture), memory, and motivational state (e.g., hunger).

■ **Chemosensory Receptors Outside of the Nose or Oral Cavity:** Localize, describe, and characterize the function of gustatory and olfactory receptors found in the gastrointestinal tract, lungs, or other areas outside the traditional locations in the oral and nasal cavities.

■ **Sentinel/Sensory Functions:** Describe how chemical senses help us avoid dangers such as spoiled or contaminated foods, how they detect potentially toxic chemicals in the environment and in our bodies, and how these protective functions can be damaged and regenerated.

■ **Genetic Aspects of Chemosensory Sensitivity:**

- Genomics: Identify genes involved in the development and normal function of the taste and smell systems.
- Variation: Describe the normal variation in taste and smell sensitivity. Identify the genes involved in order to understand what is outside the range of normal function. Describe how such variation may relate to susceptibility for human communication disorders.
- Experience: Identify genes involved with storing memories of taste and smell. Determine how experience influences future diet.
- Epigenetics: Describe how external factors (e.g., diet, stress) activate and deactivate genes.

■ **Central Control of Taste and Smell:** Characterize inputs from the central nervous system that adjust the sensitivity of taste and smell receptors or otherwise modulate sensory input, and determine how such activity may change depending on motivational or cognitive factors.

■ **Developing Tools to Measure Taste and Smell Function:** Provide practicing physicians with standardized tools to test taste and smell during physical exams or routine office visits.

■ **Develop Novel Approaches to Alter Taste Function:** Alter the levels of salt, sugar, and fat intake using innovative methods such as using artificial substitutes or changing learned flavor preferences.

■ **Training:** Emphasize training in certain classical areas of investigation (e.g., psychophysics, *in vivo* extracellular recordings, and quantitative electron microscopy) to ensure that taste and smell research can continue to be multidisciplinary.

## 2 PRIORITY AREA
### Understanding Diseases and Disorders

■ **Genetic Disorders:** Clarify and classify taste and smell disorders caused mainly by significant genetic alterations (e.g., ciliopathies and channelopathies).

■ **Sinusitis/Rhinitis:** Identify the molecular and cellular bases for loss of olfaction following nasal cavity or sinus infection, the most common cause of temporary and permanent olfactory loss.

■ **Understanding How the Activity of the Chemical Senses Can Lead to Excessive Consumption:** Determine whether excessive calorie intake is affected by normal variation or altered function of taste and smell activity.

■ **Epidemiology:** Describe the incidence and prevalence of taste and smell loss and dysfunction. For example, as the population ages, determine how many more people report taste and smell problems that affect quality of life.

## 3 PRIORITY AREA
### Improving Diagnosis, Treatment, and Prevention

■ **Improved Diagnostic Tools and Pharmacological Treatments:** Develop and validate tests to evaluate taste and smell function that are practical and affordable for use in the office setting. Develop targeted drugs to treat taste and smell dysfunction, especially drugs which slow apoptosis (cell death) and promote regeneration.

■ **Regenerative Medicine/Tissue Engineering:** Increase understanding of the properties that enable stem cells in the peripheral taste and smell pathways to proliferate and differentiate, providing insights not only for the treatment of taste and smell loss but also for the treatment of other neurological diseases.

■ **Enhancing the Clinical Enterprise:** Promote clinical training in the chemical senses, and create targeted funding opportunities, to encourage more clinical research and interdisciplinary teams of clinicians and basic scientists.

## 4 PRIORITY AREA
## Improving Outcomes for Human Communication

■ **Translational Research:** Translational Research is in its infancy in the chemical senses, due in part to the modest amount of clinical research that has been conducted. Currently, there are no evidence-based preventive measures, interventions, or treatments applied to taste and smell dysfunction. Comparative effectiveness research is premature because of the lack of intervention and treatment strategies and decisions. This is a critical gap area in the chemical senses, especially since taste and smell loss become increasingly common in a population with an increasing number of older adults.

# Voice, Speech, and Language Research

## Why NIDCD Supports Voice, Speech, and Language Research

Communication allows us to participate in society and is a defining characteristic of what it is to be human. Other organisms clearly communicate; however, in no other species does it appear that communication—specifically the use of language in communication—is as highly developed as in humans, nor as central to an organism's function and identity. Communication impairments that involve voice, speech, or language often limit a person's ability to participate in society, whether the activity is educational, occupational, or social. In addition, because effective communication is needed to get aid in life-threatening situations, loss of communication can put people at risk for compromised physical safety and survival.

Human communication systems rely on the sensory functions of the peripheral organs responsible for hearing, balance, taste, and smell, located in the middle and inner ear, nose, mouth, and throat. They also involve vision (used for sign language and visible speech) and the development of abstract linguistic representations and memory mechanisms, located centrally in the brain. Additionally, communication systems rely on the motor functions of the hands and arms (for sign language and co-speech gesture) and on the peripheral organs of speech production, which include the diaphragm, vocal folds, tongue, lips, and other oral structures. These structures are involved in other important processes such as swallowing, which can be impaired in many of the same diseases or disorders that affect speech.

Human communication requires the brain's interpretation of the complex sensory signals collected by the peripheral organs and the production of signals to choreograph the muscles involved in speaking and signing. The interplay between central and peripheral signals, genetics, and environment make language acquisition a vulnerable process. The causes of many voice, speech, and language disorders remain poorly understood and the path to treatment is often uncertain. Gaps in evidence for age-appropriate clinical goals, targets of intervention, and expected trajectories of change challenge the development of effective treatment. Researchers are only beginning to understand in sufficient detail the developmental course of speech and language markers during childhood that serve as a guide for clinical interventions suited to particular levels of development. In addition, greater documentation is needed on the decline in speech and language due to aging in order to assess clinical intervention targets for sensory and speech, language, or voice disorders.

While spoken language is the primary way people communicate, it is not the only way. The symbolic nature of language allows us to attribute meaning through not only the voice, speech, and hearing, but also using visual-manual modes of communication, most notably the use of sign languages and augmentative communication systems. NIDCD supports research to understand these communication systems, their acquisition and development, and their use when spoken language systems are damaged by trauma or degenerative diseases and disorders, or when speech is difficult to acquire due to early hearing loss or damage to the nervous system. Enhanced understanding of visual-manual language systems opens a window into general human cognition.

Voice, speech, or language impairments affect a wide range of educational, economic, and personal and public health areas. Some disorders affecting communication and swallowing are associated with substantial health-related morbidity and mortality. For example, swallowing impairments commonly lead to pneumonia, malnutrition, dehydration, and even death.[100, 101]

## INFANCY AND CHILDHOOD

Hearing loss in infancy and childhood gives rise to difficulties in acquiring spoken and written language skills. Children who are deaf are at great risk for delays in learning to read. Only 10 percent of deaf students graduate from high school reading above the eighth grade level[102] and approximately 60 percent of deaf students graduating from high school read at or below the fourth grade level.[103] Low proficiency in reading and writing limits job opportunities and economic success.

In children, language impairment and delayed language acquisition are highly significant predictors of future academic, social, vocational, and adaptive outcomes.[104-106] These impairments also tend to run in families,[107] with converging evidence of genetic effects.[108]

Many communication disorders, such as specific language impairment (SLI) and autism spectrum disorder (ASD), first become apparent during early childhood when normal language acquisition takes place. One of the hallmarks of ASD is the diminished ability to communicate effectively—particularly in the expression and reception of language. NIDCD is committed to supporting research efforts to improve the diagnosis of ASD and SLI and to develop new, or improve existing, treatments of language deficits in children with ASD and SLI, especially school-aged children with ASD who remain non-verbal and school-aged children with SLI.

## OCCUPATIONAL VOICE USERS

About three to nine percent of Americans have a voice disorder.[109] Occupational voice users such as teachers, who represent one of the country's largest employed groups, are particularly vulnerable. It is estimated that 11-38 percent of teachers have a voice problem on any given day,[110-112] and cumulative estimates indicate nearly 60 percent of teachers have been affected over their working lives.[110] Considering the impact of voice disorders for teachers—their diagnosis, treatment, and substitute teacher costs—the burden to the American economy is substantial, estimated to approach $3 billion annually in 1998.[113]

## OLDER ADULTS

A 2009 study[114] of seniors living independently showed that nearly one in five reported a voice problem, and about one in eight experienced difficulties in swallowing. These results demonstrated that severely affected individuals had reduced quality of life measures, even though only one in five of these individuals had sought treatment. Another study[115] demonstrated that approximately 50 percent of seniors living independently had a hearing loss and they were significantly more likely to experience a voice problem. These studies demonstrate a need to simultaneously manage hearing loss and voice problems in older adults.

Stroke is a leading cause of adult disability in the United States.[116] A significant proportion of stroke survivors have communication disorders (i.e., post-stroke aphasia) related to brain damage. The presence of such communication problems is a strong predictor of poor quality of life and decreased community participation.[117] NIDCD supports research to understand the neurological bases of stroke-related language and swallowing deficits, the correlation of brain imaging data with prognosis, and the development of novel intervention strategies to improve outcomes.

## THE VOICE, SPEECH, AND LANGUAGE PROGRAM

The NIDCD Voice and Speech Program performs and supports research to determine the nature, causes, treatment, and prevention of disorders of motor speech production throughout the lifespan. The Language Program is exploring the genetic bases of child speech and language disorders, as well as characterizing the linguistic and cognitive deficits in children and adults with language disorders. Both programs utilize a wide range of research approaches, including animal models of communication, to develop effective diagnostic and intervention strategies for people with voice, speech, or language impairments.

# Recent Advances in Voice, Speech, and Language Research

## TRANSFORMATIVE GENETIC STUDIES

- Scientists have discovered and confirmed the genetic basis of speech and language disorders such as stuttering[118] and SLI108 that previously were believed to be purely behavioral. These discoveries are likely to improve the classification, diagnosis, and treatment of language, reading, and speech disorders. They may also serve to reduce the stigma that individuals are "not trying hard enough," which is often associated with these disorders.

## BEHAVIORAL PHENOTYPING

- Researchers have identified distinct and viable language phenotypes that may be used in future genetic studies.[119, 120] The development of these classification systems will guide future investigations into the genetic, neurologic, and other causal factors that contribute to voice, speech, and language impairments.

## INTERVENTIONS

- Studies have demonstrated the clinical benefit of behavioral treatments, such as exercise-based treatment programs for speech and voice disorders.[121]

- Tissue engineering techniques have been established as a treatment strategy for laryngeal reconstruction in animal models of disease.[122]

- Researchers have verified the presence of biological evidence of adaptive plasticity as a function of treatment for communication disorders associated with brain injury or disease.[123, 124]

- Evidence has been found for the involvement of cognitive processes (i.e., short-term memory, attention, and executive functions) in language processing.[125, 126] In addition, evidence for the use of supplemental treatments such as neurofeedback, medications, and deep brain stimulation for cognitive disorders is expanding.[127, 128] These discoveries will leverage existing knowledge and inform the development of new treatment paradigms for voice, speech, and language impairments.

## BIOENGINEERING ADVANCES

- Scientists have developed computational and neural models of speech production and perception to predict brain activation patterns in both normal and disordered speech.[129, 130]

- Researchers have developed brain computer interface (BCI) technology, the neural control of a computer through a point and click interface that supports communication.[131, 132]

## IMAGING CORRELATIONS

- Clinical sub-phenotypes of primary progressive aphasia have been correlated with distinct brain changes.[133]
- Brain imaging has been used to identify evidence of neuro-cognitive dysfunctions underlying non lesion-specific brain disorders, such as ASD.[134]
- Novel imaging strategies that facilitate connectivity mapping have been developed to define the complex neural circuits involved in speech and language (both spoken and signed).[135]

## DEVELOPMENTAL TIMING

- Longitudinal studies have characterized brain development from infancy through adolescence, documenting a long developmental trajectory of brain development for the neural, muscular, and anatomic factors that underlie speech motor control and language.[136]
- Researchers understand better both functional and structural brain plasticity associated with normal learning, hearing loss, and maladaptation in certain disorders.[137] Such findings may inform the development of new treatment paradigms.

## SCIENCE CAPSULE
### Primary Progressive Aphasia

Primary progressive aphasia (PPA) is a type of dementia defined by the gradual loss of language abilities as the principal feature of a degenerative disease of the brain. First identified as a distinct disorder in 1982, PPA differs from other dementias, such as Alzheimer's disease, because the language deficit is present during early phases of the disease in the absence of memory problems, other cognitive deficits, or traumatic brain injury. PPA is divided into three clinical subtypes: agrammatic (difficulty with word order), semantic (difficulty understanding words, but word production is near normal), or logopenic (difficulty with word finding, resulting in halted speech).

In recent years, significant progress has been made in discriminating between people with PPA and other dementias, and between the subtypes of PPA. In 2009, NIDCD-supported scientists identified a series of word performance tasks that discriminate quantitatively between the three clinical subtypes of PPA.[138] In addition, the individuals categorized using this methodology showed specific and different brain regions that had atrophied in correlation with the subtype. These results provide a foundation for researchers and clinicians to be able to predict the likely progression of PPA, such as whether affected people will go on to develop additional dementias or experience other neurodegenerative deficits.

While a drug therapeutic has not yet been proven effective to treat PPA through a clinical trial, case reports have demonstrated rapid improvement in symptoms for specific individuals.[139] Behavioral interventions have also been effective in case studies.[140] These case reports provide hope for affected people and their families that future research will validate these or other interventions and provide a template for treatment.

# Priority Areas in Voice, Speech, and Language Research

The NIDCD Voice, Speech, and Language Program contains areas of research that overlap with mission areas of other NIH ICOs. For example:

- **Language:** The normal acquisition of language is within the mission area of the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD). Additionally, normal language decline as a result of normal aging is within the mission of the National Institute on Aging (NIA). NIDCD research focuses on language acquisition in the presence of dysfunctions, diseases, and disorders that alter the traditional developmental course such as hearing loss, ASD, SLI, and aphasia.

- **Literacy:** As with language, the normal acquisition of literacy skills and individual outcomes in educational settings are within the mission of NICHD. NIDCD supports research into literacy for people who are deaf and HoH, the acquisition of written language for people with pre-existing language disorders, and educational interventions to support improved individual outcomes.

- **Swallowing:** Speech and swallowing functions have some shared structures, leading NIDCD to fund research on swallowing and disordered swallowing (dysphagia). Dysphagia often occurs as a result of a disease process such as neurologic conditions or head and neck cancer. Therefore, many NIH ICOs, such as NIDDK, NIA, NINDS, NCI, NICHD, the National Institute of Dental and Craniofacial Research (NIDCR), and the National Institute of Nursing Research (NINR), share an interest with NIDCD in research on swallowing and dysphagia.

## 1 PRIORITY AREA
### Understanding Normal Function

- **Laryngeal System:** Examine effects of laryngeal muscle function and structure (e.g., muscle fiber and mucosal changes) on vocal health, in particular with respect to voice training and vocal dose—the amount, intensity, and distribution of voice use.

- **Motor Speech Production:** Determine the similarities and differences in development and functioning of neural and musculoskeletal systems for human voice and speech production vs. non-speech oral motor control in order to identify the sensorimotor principles underlying typical speech development and adult speech motor control.

- **Databases:** Establish normative databases through the human lifespan for anatomic, acoustic, and physiologic measures that have clinical application for voice, speech, and language.

- **Developmental Plasticity:** Identify behavioral changes, sensory and motor plasticity, and the underlying neural mechanisms associated with voice and speech motor learning in children (e.g., sensorimotor adaptation).

- **Sign Language Research:** Investigate the acquisition, processing, and neural underpinnings of languages within the visual-manual modality.

- **Literacy and Deafness:** Identify factors associated with the successful comprehension and use of written language for people who are deaf.

## 2 PRIORITY AREA
## Understanding Diseases and Disorders

- **Genetics:** Identify genetic and epigenetic factors that contribute to voice, speech, and language impairments.

- **Neural Plasticity:** Examine changes in brain structure and functioning in response to behavioral, pathologic, or environmental insult as a basis for voice, speech, and language impairments.

- **Epidemiology:** Identify genetic, neural, sensorimotor, cognitive, linguistic, behavioral, demographic, and environmental factors associated with voice, speech, and language impairments. Determine the relative contribution of those factors to risk for development of, or recovery from, impairment.

- **Pathophysiology:** Identify the pathophysiologic and cognitive mechanisms underlying voice, speech, and language impairments.

- **Natural History:** Determine the progression and developmental course of voice, speech, and language impairments.

- **Co-Occurring Conditions:** Examine factors (e.g., social context, inflammatory response) that interact or coexist with primary voice, speech, and language impairments. Examine diagnostic and treatment strategies for voice, speech, and language impairments that may coexist in individuals with deafness.

## 3 PRIORITY AREA
### Improving Diagnosis, Treatment, and Prevention

- **Biomarkers:** Develop biomarkers (e.g., genetic, imaging) to support diagnosis, improve accuracy of prognosis, improve treatments, or monitor response to treatment of voice, speech, and language impairments.

- **Hypothesis-Driven Interventions:** Develop models of intervention informed by cognitive, linguistic, biological, or neurophysiological processes, accounting for cultural and linguistic variation.

- **Efficacy:** Using outcomes-based clinical studies and randomized clinical trials, determine the efficacy of proposed interventions for the prevention and treatment of voice, speech, and language impairments.

- **Prevention:** Develop programs that prevent the onset or limit the severity of voice, speech, and language impairments for people with genetic, occupational, environmental, or other risks.

- **Improving Literacy in Deaf Individuals:** Develop methods that promote the acquisition of literacy skills during childhood and improve the reading and writing abilities of people who are deaf and have limited literacy.

- **Understudied Populations:** Develop new interventions or approaches for understudied populations (e.g., school-aged, minimally-verbal children with ASD) or conditions (e.g., stuttering and apraxia of speech in children and adults).

- **Assistive Technologies:** Harness recent advances in bioengineering to inform the development of novel augmentative and alternative communication (AAC) approaches and to enhance BCI technologies for communication.

- **Training:** Promote the cross training of basic scientists, clinician scientists, and physician scientists to facilitate the development of interdisciplinary research teams and to stimulate translational research.

## 4 PRIORITY AREA
## Improving Outcomes for Human Communication

**Novel Delivery:** Translate conventional interventions into new delivery models (e.g., group, family, telehealth, emerging technology platforms).

**Screening:** Develop effective and efficient clinical screening tools for use in health and community settings such as schools, primary care physician offices, and senior centers.

**Comparative Effectiveness Research and Evidence-Based Medicine:** Through clinical trials and epidemiological comparative effectiveness research, identify best treatments for a given communication disorder for a defined set of individuals. Develop and use clinical registries, clinical data networks, and other forms of electronic health data to inform the conscientious, explicit, and judicious use of current best evidence in making decisions about health care options to improve outcomes for individuals with communication disorders.

**Community-Based Research:**

- Promote community-based research and data collection to identify factors that influence outcomes for people with voice, speech, or language impairments, and to inform the development of public policy recommendations.
- Examine community-level health promotion strategies to prevent the occurrence of, reduce the risk of, or improve the adherence with treatment of voice, speech, and language impairments.

**Training:**

- Train clinicians and physicians (e.g., speech-language pathologists, otolaryngologists) in the science knowledge base to enhance uptake of new research findings into practice.
- Develop a cadre of science dissemination experts in voice, speech, and language to hasten the translation of research advances to routine community practice.

**Bridging the Gap between Research and Practice:** Determine effective dissemination and implementation strategies that enhance the adoption of voice, speech, and language clinical discoveries into routine community practice.

# Summary

The mission of the NIDCD is to conduct and support biomedical and behavioral research and research training in the normal and disordered processes of hearing, balance, taste, smell, voice, speech, and language. The Institute also conducts and supports research and research training related to disease prevention and health promotion; addresses special biomedical and behavioral problems associated with people who have communication impairments or disorders; and supports efforts to create devices that substitute for lost and impaired sensory and communication function.

The goals listed in the NIDCD Strategic Plan are an assessment of research areas that present the greatest scientific opportunities and public health needs over the next five years for the three program areas: hearing and balance; taste and smell; and voice, speech and language. The goals in the Strategic Plan's Priority Areas are a guide for:

- Scientists: To better understand the directions that NIDCD research may take in the future;
- The NIDCD: To assist in developing FOAs and to identify projects for HPP nomination; and
- The Public: To understand the state of communication sciences and to discover the scientific breakthroughs that are possible with sustained investments in biomedical research.

The Plan is not a complete list of all research areas that the NIDCD is currently supporting or plans to support in the future. The NIDCD is committed to supporting new, innovative, hypothesis-driven, meritorious research; however, the Plan will assist us in identifying research areas that have a great opportunity to help the NIDCD improve the health and quality of life of people with communication disorders.

# Appendix A: NIDCD Funding History

Appropriated funds for NIDCD increased dramatically in the first 15 years after the establishment of the Institute in FY 1989. Funding for NIDCD has remained fairly constant since FY 2005, and even with constrained budgets, NIDCD sustained only a 0.89 percent decrease in FY 2011. An additional $102.9 million was appropriated to NIDCD for FY 2009 through the American Recovery and Reinvestment Act (ARRA) (Figure 1.) (For more information on ARRA, go to http://www.nidcd.nih.gov/funding/ARRA/ and http://www.recovery.gov.)

## NIDCD CONGRESSIONAL APPROPRIATIONS AND ARRA OBLIGATIONS

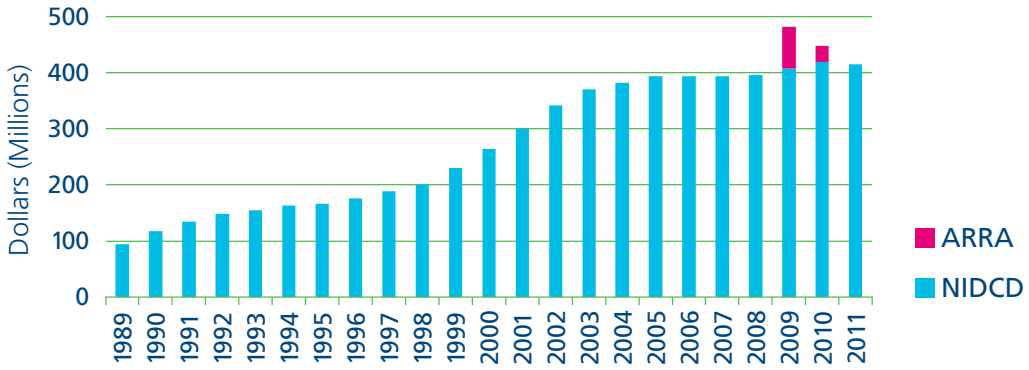



Figure 1: Annual Congressional Appropriations for NIDCD. ARRA funding was appropriated in 2009, but was obligated in FY 2009 and FY 2010. Data compiled by the NIH Office of Budget (http://officeofbudget.od.nih.gov/approp_hist.html.)

NIDCD funds extramural and intramural research in hearing, balance, taste, smell, voice, speech, and language (Figure 2.)

## TOTAL NIDCD OBLIGATED FUNDS FY 2011

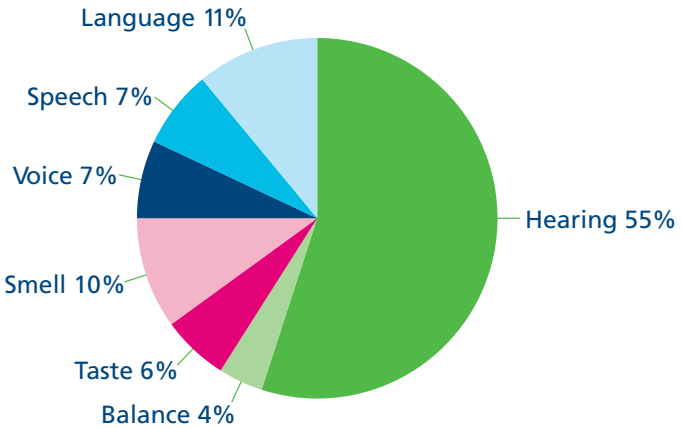



Figure 2: Total NIDCD obligated funds (excluding ARRA funding) include extramural research, intramural research, and research management and support (RMS.) FY 2011 obligated funds data compiled by the NIDCD Financial Management Branch.

# Appendix B: Trans-NIH Activities

## NIDCD PARTICIPATES IN THE FOLLOWING TRANS-NIH RESEARCH ACTIVITIES:

**NIH Autism Coordinating Committee**
(http://www.nimh.nih.gov/health/topics/autism-spectrum-disorders-pervasive-developmental-disorders/nih-initiatives/nih-autism-coordinating-committee.shtml): At the request of Congress, seven NIH ICOs formed the Autism Coordinating Committee (NIH/ACC) to enhance the quality, pace, and coordination of efforts at NIH to find a cure for autism. The NIH/ACC has been instrumental in advancing research to understand ASD. Member ICOs fund 11 Autism Centers of Excellence, host workshops, and publish FOAs that encourage new discoveries for the prevention, diagnosis, and treatment of ASD. The NIH/ACC is also integrally involved in the broader federal Interagency Autism Coordinating Committee (IACC) (http://iacc.hhs.gov/), which is composed of representatives from various component agencies of HHS and other departments. The NIDCD Director serves as a member of the IACC.

**NIH Basic Behavioral and Social Science Opportunity Network (OppNet)**
(http://oppnet.nih.gov/): The mission of OppNet is to pursue opportunities for strengthening basic behavioral and social science research (b-BSSR) at the NIH. OppNet advances b-BSSR through activities and initiatives that build a body of knowledge about the nature of behavioral and social systems. Twenty-nine NIH ICOs integrate existing NIH efforts, target research challenges best met collectively, and collaborate on new research initiatives in complementary scientific areas. OppNet also relies on its stakeholders, who have provided scientific perspectives through a Request for Information and a public conference in 2010.

**NIH Blueprint for Neuroscience Research**
(http://neuroscienceblueprint.nih.gov/): The NIH Blueprint is a collaborative framework of 16 NIH ICOs that support research on the nervous system. By pooling resources and expertise, the NIH Blueprint identifies crosscutting areas of research, and confronts challenges too large for any single NIH ICO. Since its inception in 2004, the Blueprint has supported the development of new tools, training opportunities, and other resources to assist neuroscientists. These resources include:

- **The Gene Expression Nervous System Atlas (GENSAT)** (http://www.gensat.org/index.html) and the Cre Driver Network (http://www.credrivermice.org/) are projects to develop, characterize, and distribute transgenic mouse lines to serve as tools for research on the nervous system.
- **The Neuroimaging Informatics Tools and Resources Clearinghouse (NITRC)** (http://www.nitrc.org/) is a web-based clearinghouse that helps researchers find and compare neuroimaging informatics tools and resources.
- **The Neuroscience Information Framework (NIF)** (http://www.neuinfo.org/) is an online portal for neuroscience information that includes a customized search engine, a curated registry of resources, and direct access to more than a dozen online databases.

- **The NIH Toolbox for Assessment of Neurological and Behavioral Function** (http://www.nihtoolbox.org/) initiative seeks to assemble brief, comprehensive assessment tools that will be useful to clinicians and researchers in a variety of settings, with a particular emphasis on measuring outcomes in longitudinal epidemiologic studies and prevention or intervention trials across the lifespan.

### NIH Knockout Mouse Project (KOMP)

(http://www.nih.gov/science/models/mouse/knockout/index.html): The Knockout Mouse Project is a Trans-NIH initiative of 19 ICOs that is building a public repository of mouse embryonic stem cells containing "knocked out" or inactivated genes for nearly every gene in the mouse genome. This comprehensive resource of knockout mice is already benefitting the biomedical research community and enhancing our understanding of human disease. KOMP is one of the Trans-NIH Mouse Initiatives (http://www.nih.gov/science/models/mouse/), an effort co-chaired by NIDCD Director Dr. James Battey. These programs have direct application for many NIDCD researchers, allowing them to ask questions about specific genetic defects to determine their impact on the development of, and potential recovery from, deafness and other communication disorders.

### Trans-NIH Zebrafish Initiative

(http://www.nih.gov/science/models/zebrafish/): The zebrafish (*Danio rerio*) is a unique vertebrate model that has a number of significant benefits for NIDCD's mission areas. Perhaps the most exciting feature of the zebrafish anatomy is the presence of the lateral line, a line of easy-to-access hair cell-like sensory cells that develop along both sides of the fish. In addition, the zebrafish is transparent during much of early development, allowing easier observation of its developing sensory systems. The Zebrafish Initiative promotes the use of the zebrafish as a model organism for the study of vertebrate development and disease through the support of courses and meetings, genetic and genomic resources, reports and publications, and research initiatives.

# Appendix C: The NIDCD 2012-2016 Strategic Plan: The Process

In the fall of 2010, NIDCD's Science Policy and Planning Branch (SPPB) began the process of rewriting the current NIDCD Strategic Plan for research, which was expiring in 2011. SPPB staff reviewed current and previous NIDCD Strategic Plans for Research, as well as those of other ICOs. Based on this review, SPPB implemented several initiatives in developing the new Plan:

### 1. CONVERTED TO A FIVE-YEAR PLAN RATHER THAN A THREE-YEAR PLAN

To match the majority of the other NIH ICO's Strategic Plans, to allow for more long-term goals, and to reduce the burden of staff time, SPPB extended the time period of the Plan to five-years to cover the period of 2012-2016. The five-year Plan is expected to encourage the achievements of scientific short- and medium-range projects (e.g., R01, R03, R21) as they move toward the long-range goals stated in the Plan.

### 2. ISSUED REQUEST FOR INFORMATION (RFI)

On September 2, 2010, SPPB published a Request for Information (RFI) notice NOT-DC-10-001 (http://grants.nih.gov/grants/guide/notice-files/NOT-DC-10-001.html) in the NIH Guide for Grants and Contracts. The RFI provided an opportunity for the scientific and advocacy communities and members of the public to engage in the NIDCD strategic planning process at an early stage. On November 3, 2010, NIDCD published NOT-DC-11-002 (http://grants.nih.gov/grants/guide/notice-files/NOT-DC-11-002.html), "Notice of Extension for Request for Information: National Institute on Deafness and Other Communication Disorders (NIDCD) Strategic Plan Update." NOT-DC-11-002 extended the original response date from November 5, 2010, to December 5, 2011.

In preparation for rewriting the NIDCD Strategic Plan, NIDCD used the RFI to seek information on four questions:

1. What are the most significant scientific discoveries in the communication sciences that have occurred in the past decade? (Please provide reference(s) to scientific journal article(s), if applicable)
2. What are the gaps in current research and training in the communication sciences?
3. What pressing needs of individuals with communication disorders can be helped with additional research?
4. What are the greatest challenges or barriers to progress in the communication sciences?

NIDCD received 38 comments during the RFI comment period. Two comments requested health information and were excluded from the list of 36 remaining comments.

Subsequently, the Chemical Senses and Voice, Speech, and Language Working Groups sent out the RFI questions again in January and February 2011, to scientific societies in which they held membership. As a result, NIDCD received 20 additional responses.

### 3. CONVENED SCIENTIFIC EXPERT WORKING GROUPS

SPPB hosted separate working groups for each of the three main program areas (Hearing and Balance; Chemical Senses; Voice, Speech, and Language) in March 2011. To establish each working group, the relevant NIDCD program officers identified seven to ten outside scientific experts and invited them to serve on the working group. The rosters of each of the working groups are on pages 48-49. Co-chairs were also selected for each working group, as well as a current NDCD Advisory Council member to serve as Council Liaison. SPPB and other NIDCD staff served as resource persons before, during, and after the working group meetings. Prior to the meetings, working group participants received instructions (including RFI summaries, pre-writing assignment suggestions, and roster/contact information of working group members and NIDCD staff) along with an NIDCD grant portfolio analysis for their respective program area. The scientific experts spent time during the working group meetings identifying areas of outstanding opportunity and unmet need within their areas of expertise. Following the working group meetings, SPPB staff used workshop summaries to develop a first draft of the new Plan.

### 4. PRESENTED TO NDCD ADVISORY COUNCIL

NIDCD invited each of the Council Liaisons to present their working group's recommendations at the May 2011 meeting of the NDCD. The NIDCD then incorporated the Council's revisions into the draft Plan. At the September 2011 NDCD Advisory Council meeting, NIDCD staff presented a revised version of the draft Plan, received additional comments from Council members, and incorporated these revisions into the next draft.

### 5. SOLICITED PUBLIC COMMENTS

The draft Plan was made available for a 30-day Public Comment Period on the NIDCD website in the fall of 2011. To announce the public comment period, the NIDCD published the Notice NOT-DC-12-001 (http://grants.nih.gov/grants/guide/notice-files/NOT-DC-12-001.html) in the *NIH Guide for Grants and Contracts* on October 21, 2011. The NIDCD also published a Notice in the Federal Register on October 27, 2011 (http://www.federalregister.gov/articles/2011/10/27/2011-27823/national-institute-on-deafness-and-other-communication-disorders-draft-2012-2016-strategic-plan.)

NIDCD received 34 comments. Three comments were duplicates and one comment requested health information. These four were excluded from the list of 30 remaining comments.

### 6. FINALIZED AND POSTED THE PLAN ON THE NIDCD WEBSITE

Once appropriate Public Comments were incorporated into the draft approved by NIDCD staff, SPPB finalized the Plan and published it on the NIDCD website in early 2012.

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# Appendix D: Glossary and Acronym List

## GLOSSARY

| TERM | DEFINITION |
|---|---|
| **afferent** | conducting toward the center; for neurons, conducting nerve impulses toward the spinal cord and brain |
| **aphasia** | total or partial loss of the ability to use or understand language; usually caused by stroke, brain disease, or injury |
| **apraxia of speech** | a speech disorder, also known as verbal apraxia or dyspraxia, in which a person has trouble speaking because of inability to execute a voluntary movement despite normal muscle function |
| **assistive technologies** | products, devices, or equipment that help maintain, increase, or improve the functional capabilities of people with disabilities |
| **auditory nerve** | eighth cranial nerve that connects the inner ear to the brainstem and is responsible for hearing and balance |
| **auditory system** | the outer, middle, and inner ear, along with the neurons and brain regions involved in hearing |
| **autism spectrum disorders** | a spectrum of developmental disorders that begin in early childhood and persists throughout adulthood; autism spectrum disorders affect three crucial areas of development: communication, social interaction, and creative or imaginative play |
| **biofilm** | colonies of antibiotic-resistant bacteria that are present in the middle ears of most children with chronic ear infections |
| **biomarker** | a specific physical trait or a measurable biologically produced change in the body connected with a disease or health condition |
| **central auditory system** | neural circuitry and brain regions involved in processing sound |
| **chemesthesis** | the "feel" of a chemical; the term describes chemically provoked irritation |

| | |
|---|---|
| **chemical senses** | taste and smell; see "gustation" and "olfaction" |
| **cochlea** | see "inner ear" |
| **cochlear implant** | a medical device that bypasses damaged structures in the inner ear and directly stimulates the auditory nerve, allowing some people who are deaf or HoH to learn to hear and interpret sounds and speech |
| **comorbid** | the existence of one or more co-occurring disorders in addition to a primary disorder |
| **efferent** | conducting away from the center; for neurons, conducting outward from the spinal cord and brain |
| **embryonic stem cells** | cells that are derived from the inner cell mass of blastocyst stage embryos, are capable of dividing without differentiating for a prolonged period in culture, and are known to develop into cells and tissues of the three primary germ layers |
| **epigenetics** | the study of heritable changes caused by the activation and deactivation of genes without any change in the underlying DNA sequence of the organism |
| **eustachian tube** | a small passageway that connects the upper part of the throat to the middle ear; its job is to supply fresh air to the middle ear, drain fluid, and keep air pressure at a steady level between the nose and the ear |
| **gene expression** | the process by which the information encoded in a gene is used to direct the assembly of a protein molecule; different subsets of genes are expressed in different cell types or under different conditions |
| **genetics** | the study of particular genes, DNA, and heredity |
| **genomics** | the study of the genome (the entire genetic makeup) of an organism |
| **gustation** | tasting; the sensation produced by a stimulus applied to the gustatory nerve endings in the tongue |
| **hair cells** | sensory cells of the inner ear, which are topped with hair-like structures (stereocilia) and which transform the mechanical energy of sound waves into nerve impulses |
| **hearing aid** | an electronic device that brings amplified sound to the ear; it usually consists of a microphone, amplifier, and receiver |

| | |
|---|---|
| **idiopathic** | relating to a disease or disorder that arises spontaneously or without a known cause |
| **induced pluripotent stem cells** | a type of pluripotent stem cell, similar to an embryonic stem cell, formed by the introduction of certain embryonic genes into a somatic cell |
| **informatics** | a sub-discipline of biology and computer science concerned with the acquisition, storage, analysis, and dissemination of biological data (most often DNA and amino acid sequences) to determine gene and protein functions, establish evolutionary relationships, and predict the three-dimensional shapes of proteins |
| **inner ear** | part of the ear that contains both the organ of hearing (the cochlea) and the organ of balance (the labyrinth) |
| **knockout** | an organism that has been genetically engineered to lack one or more specific genes; scientists study knockout organisms to determine the impact of the missing gene(s) so as to understand the function of the missing gene(s) |
| **larynx** | valve structure between the trachea (windpipe) and the pharynx (the upper throat) that is the primary organ of voice production |
| **Ménière's disease** | inner ear disorder that can affect both hearing and balance and causes a sensation of fullness in the ear along with episodes of vertigo, hearing loss, and tinnitus |
| **model organism** | animal species used in medical research to mimic aspects of a disease found in humans |
| **mutation** | a change in a DNA sequence that can result from DNA copying mistakes made during cell division, exposure to ionizing radiation, exposure to chemical mutagens, or infection by viruses |
| **neural prostheses** | devices such as the cochlear implant that substitute for an injured or diseased part of the nervous system |
| **olfaction** | smell; to perceive odor or scent through stimuli affecting the olfactory nerves |
| **otitis media** | inflammation of the middle ear caused by infection |

| | |
|---|---|
| **pathogenesis** | the development of a disease or condition, particularly the cellular and molecular origins and causes of disease development |
| **peripheral auditory system** | the components of the outer, middle, and inner ear involved in hearing |
| **phenotype** | an individual's physical and behavioral characteristics |
| **polymorphism** | one of two or more variants of a particular DNA sequence that can correlate with disease, drug response, and other phenotypes; the most common type of polymorphism involves variation at a single base pair (single nucleotide polymorphism) of DNA |
| **proprioception** | the ability to sense the position, location, orientation, and movement of the body and its parts |
| **psychophysics** | the study of the relationship between physical stimulus and perception |
| **rhinitis** | inflammation of the mucous membranes of the nose, generally accompanied by discharge (runny nose) and usually caused by a virus infection (e.g., the common cold) or by an allergic reaction (e.g., hay fever) |
| **sinusitis** | inflammation or infection of one of the air-filled nasal sinuses |
| **spasmodic dysphonia** | momentary disruption of voice caused by involuntary movements of one or more muscles of the larynx |
| **spiral ganglion** | the group of nerve cells that serve the sense of hearing by sending a representation of sound from the cochlea to the brain; the cell bodies of the spiral ganglion neurons are found in the spiral structure of the cochlea |
| **stereocilia** | see "hair cells" |
| **stria vascularis** | specialized epithelium lining the cochlear duct that maintains the ion homeostasis of the fluid within the cochlea |
| **stuttering** | a speech disorder in which sounds, syllables, or words are repeated or prolonged, disrupting the normal flow of speech |

| | |
|---|---|
| **tinnitus** | sensation of a ringing, roaring, or buzzing sound in the ears or head when no actual sound stimulus is present in the environment |
| **tonotopic** | the spatial arrangement of where sounds of different frequency are processed in the brain. For example – the auditory nerves that carry signals from adjacent portions of the cochlea project their information to adjacent portions of the auditory cortex |
| **transduction** | the process by which stimuli in the environment are converted into electrical (neural) signals by sensory receptors |
| **transgenic** | having one or more DNA sequences from another species introduced by artificial means |
| **vertigo** | illusion of movement; a sensation as if the external world were revolving around an individual (objective vertigo) or as if the individual were revolving in space (subjective vertigo) |
| **vestibular system** | system in the body that is responsible for maintaining balance, posture, and the body's orientation in space; this system also regulates locomotion and other movements and keeps objects in visual focus as the body moves |

## ACRONYMN LIST

| | |
|---|---|
| **AAC** | Augmentative and Alternative Communication |
| **ABI** | Auditory Brainstem Implant |
| **ACC** | Autism Coordinating Committee |
| **ARRA** | American Recovery and Reinvestment Act |
| **ASD** | Autism Spectrum Disorder |
| **Au.D.** | Doctor of Audiology |
| **b-BSSR** | Basic Behavioral and Social Science Research |
| **BCI** | Brain Computer Interface |
| **BDNF** | Brain-Derived Neurotrophic Factor |
| **BPPV** | Benign Paroxysmal Positional Vertigo |
| **CDC** | Centers for Disease Control and Prevention |
| **DEA** | Division of Extramural Activities |
| **DIR** | Division of Intramural Research |
| **DNA** | Deoxyribonucleic Acid |
| **DSP** | Division of Scientific Programs |
| **FDA** | Food and Drug Administration |
| **FOA** | Funding Opportunity Announcement |
| **FPR** | Formyl Peptide Receptors |
| **FY** | Fiscal Year |
| **GENSAT** | Gene Expression Nervous System Atlas |
| **HHS** | U.S. Department of Health and Human Services |
| **HoH** | Hard of Hearing |
| **HPP** | High Program Priority |
| **IACC** | Interagency Autism Coordinating Committee |
| **ICO** | Institutes, Centers, and Offices |
| **iPSC** | Induced Pluripotent Stem Cell |
| **KOMP** | NIH Knockout Mouse Project |
| **M.D.** | Doctor of Medicine |
| **NASA** | National Aeronautics and Space Administration |

| | |
|---|---|
| **NCI** | National Cancer Institute |
| **NDCD** | National Deafness and Other Communication Disorders |
| **NHLBI** | National Heart, Lung, and Blood Institute |
| **NF2** | Neurofibromatosis 2 |
| **NIA** | National Institute on Aging |
| **NIAID** | National Institute of Allergy and Infectious Diseases |
| **NICHD** | *Eunice Kennedy Shriver* National Institute of Child Health and Human Development |
| **NIDCD** | National Institute on Deafness and Other Communication Disorders |
| **NIDCR** | National Institute of Dental and Craniofacial Research |
| **NIDDK** | National Institute of Diabetes and Digestive and Kidney Diseases |
| **NIF** | Neuroscience Information Framework |
| **NIH** | National Institutes of Health |
| **NINDS** | National Institute of Neurological Disorders and Stroke |
| **NINR** | National Institute of Nursing Research |
| **NITRC** | Neuroimaging Informatics Tools and Resources Clearinghouse |
| **OppNet** | Opportunity Network |
| **OM** | Otitis Media |
| **PPA** | Primary Progressive Aphasia |
| **Ph.D.** | Doctor of Philosophy |
| **PKD** | Polycystic Kidney Disease |
| **Plan** | NIDCD Strategic Plan |
| **RE** | Respiratory Epithelium |
| **RFI** | Request for Information |
| **SLI** | Specific Language Impairment |
| **SPPB** | Science Policy and Planning Branch |
| **T2R** | Type 2 Taste Receptors |
| **TAAR** | Trace Amine-Associated Receptor |
| **TRIOBP** | TRIO and F-actin Binding Protein |
| **VA** | Department of Veterans Affairs |

# Appendix E: Bibliography


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NIH Publication No. 12-3711